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(54) Title: Peptides with the immunological properties of HIV-2

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The present invention relates to peptides having immunological, possibly immunogenic, properties in common with antigens capable of being obtained in a purified form, from viruses capable of causing lymphadenopathies capable of being subsequently replaced by the acquired immunodeficiency symdrome (AIDS) in man.

The invention relates, in particular, to antigenic peptides capable of being recognized by antibodies induced in man by viruses designated by the abbreviation HIV, according to the nomenclature defined in NATURE. It also relates to peptides having immunogenic properties or capable of being rendered immunogenic in vivo, this immunogenicity being capable of manifesting itself by the induction in vivo of antibodies which recognize antigens characteristic of HIV-2 viruses and, at least in the case of some of these peptides, even antigens derived from HIV-1.

The invention furthermore relates to applications of these peptides to the manufacture of compositions for in vitro diagnosis in man of potentiality of certain forms of AIDS and, in the case of some of them, to the production of immunogenic compositions and vaccine compositions against HIV retroviruses.

Likewise, the invention relates to the applications, for the same purposes, of antibodies capable of being induced in vivo by immunogenic peptides or peptides rendered immunogenic and, for some of these antibodies, to their applications to the production of active ingredients of medicinal products against human AIDS.

The invention also relates to the use of some of these peptides in processes for the in vitro diagnosis in man of some forms of AIDS, as well as to their

application to the production of diagnostic boxes or "kits".

A first retrovirus termed LAV-1 or HIV-1 has been isolated and described in Patent Application GB.83/24.800 and an Application EP.84/401.834 of 14/09/84. This virus has also been described by F. Barre Sinoussi et al. in Science, 220 No. 45-99, 20 pages 868-871.

Variants of this HIV-1 virus designated by LAV ELI and LAV MAL have also been isolated, characterized and described in Patent Application EP.84/401.834.

The HIV-1 viruses and their variants possess the following properties:

- their preferred targets are the human Leu3 cells (or T4 lymphocytes) and their "immortalized" derived cells,
- they have a reverse transcriptase activity requiring the presence of Mg^{2+} ions and possess a high activity for poly(adenylate-oligo-deoxythymidylase) poly(A)-oligo(dT)12-18)
- they have a density of 1.16 to 1.17 on sucrose gradient,
- they have a mean diameter of 139 nanometres and a nucleus with a mean diameter of 41 nanometres,
- the lysates of these viruses contain a protein p25 (nuclear protein) which does not exhibit immunological cross-reactivity with protein p24 of HTLV-1,
- they contain a protein p42 belonging to their envelope,
- they also contain an envelope glycoprotein gp110 with a molecular weight of 110,000.

The isolation and characterization of retroviruses belonging to a distinct class and having only a reduced immunological relationship with the preceding

ones, have been described in European Patent Application No. 87/400.151.4. These retroviruses which have been grouped under the designation HIV-2, have been isolated in several African patients exhibiting symptoms of a lymphadenopathy or AIDS.

The HIV-2 type retroviruses like the HIV-1 type retroviruses are characterized by a tropism for the human T4 lymphocytes and by a cytopathogenic effect towards these lymphocytes when they multiply therein, then causing either generalized and persistent polyadenopathies or AIDS.

More generally, the retroviruses purified by HIV-2 possess, in general, the following properties:

- the preferred target of HIV-2 retroviruses consists of human Leu3 cells (or T4 lymphocytes) and for "immortalized" cells derived from these T4 lymphocytes;
- they are cytotoxic for human T4 lymphocytes
- they have a reverse transcriptase activity requiring the presence of Mg^{2+} ions and possessing a high activity for poly(adenylate-oligodeoxythylmidylase) (poly(A)-oligo(dT)12-18);
- they have a density of 1.16 in a sucrose gradient;
- they have a mean diameter of 140 nanometres and a nucleus having a mean diameter of 41 nanometres;
- they can be cultured in permanent lines of the HUT type or expressing the protein T4;
- they are not infectious for T8 lymphocytes;
- the lysates of these viruses contain a protein p26 which does not exhibit immunological cross-reactivity with the protein p24 of the HTLV-I virus or HTLV-II virus;
- these lysates contain, in addition, a protein p16 which is not immunologically recognized by the

protein p19 of HTLV-I or of HTLV-II in radioimmunoprecipitation assays;

- they contain, in addition, an envelope glycoprotein having a molecular weight of the order of 130,000-140,000 which does not exhibit immunological cross-reactivity with gp110 of HIV-1 viruses, but which, on the other hand, exhibit immunological cross-reactivity with the envelope glycoprotein gp140 of STLV-III (virus isolated from monkeys);

- these lysates also contain antigens which can be labelled with ^{35}S-cysteine, the molecular weights of which antigens range between 32,000 and 42,000-45,000; they comprise especially an antigen having a molecular weight of the order of 36,000 and an antigen having a molecular weight of the order of 42,000, one of these antigens (p36 and p42) probably constituting a transmembrane glycoprotein of the HIV-2 virus;

- the genomic RNA of HIV-2 viruses does not hybridize with the genomic RNA of HIV-1 under stringent conditions;

- under non-stringent conditions, the genomic RNA of HIV-2 does not hybridize either with the env gene and the LTR adjacent to it, of HIV-1, or with sequences of the pol region of the HIV-1 genome;

- under non-stringent conditions, it hybridizes weakly with nucleotide sequences of the HIV-1 region.

Another retrovirus termed SIV-1, this name replacing the previously known name STLV III, was isolated from Rhesus macaque monkeys (M.D.Daniel et al. Science 228, 1201 (1985) N.L.Letwin et al. Science 230, 71 (1985) under the name "STLV-IIImac").

Another retrovirus, designated "STLV-III_{AGM}" (or SIV_{AGM}) has been isolated in wild green monkeys. But in contrast to the virus present in the Rhesus macaque

monkey, the presence of "STLV-III_{AGM}" does not appear to induce an AIDS type disease in the African green monkey.

A retrovirus strain SIV-1mac has been deposited at CNCM on 7 February 1986 under No. I-521. Studies have shown that the SIV-1 retrovirus comprises some proteins which possess a certain immunological relationship with structural proteins or glycoproteins capable of being obtained under similar conditions, from HIV-2. This SIV-1 retrovirus, whose infectious character has been observed in monkeys, had been designated STLVIII by the researchers who isolated it (abovementioned bibliographic references).

For simplicity of expression, these viruses will be designated hereinafter only by the expression SIV (the expression SIV is the English abbreviation for "Simian immunodeficiency virus") optionally followed by an abbreviation designating the species of monkey from which they are derived, for example MAC (or mac) for macaque or AGM for African green monkey.

By using the same techniques as those recalled above, it was observed that there could also be obtained from SIV-1mac:

- a principal nuclear protein p27, having a molecular weight of the order of 27 kilodaltons,
- a major envelope glycoprotein, gp140,
- a probably transmembrane protein p32, which is barely observed in RIPA when the virus has been labelled beforehand with ^{35}S-cysteine, but which can be observed in immunoblotting assays (Western blots), in the form of broad bands.

More precise studies have been carried out regarding the preceding HIV-2 and SIV viruses. The continuation of the study of the HIV-2 retroviruses has also led to the production of complementary DNA (cDNA)

sequences of the RNAs of their genomes. The complete nucleotide sequence of the cDNA of a retrovirus representative of the HIV-2 class (HIV-2 ROD) was deposited on 21/02/1986 at CNCM under the No. I-522, under the reference name LAV-II ROD).

This nucleotide sequence and the open reading frames which it contains are indicated in Figure 1A.

Furthermore, the continuation of the study of other retroviruses also made it possible to obtain their complete nucleotide sequences. Such is the case in particular for the cDNA derived from the SIV genomic RNA.

The cloning and the sequencing of the SIV-1mac virus, which made it possible to obtain its nucleotide sequence, were performed under the following conditions:

The DNA of HUT 78 cells infected with the SIV virus (STLV-IIImac 142-83 isolate described by Daniel et al. (1985) Science, 228, p. 1201-1204, partially digested with the restriction enzyme Sau3A was cloned into the BamHI site of the bacteriophage vector Lambda ELBL3 in order to constitute a genomic library. The 2 million recombinant phages from the genomic library thus constituted were screened in situ under the P3 safety conditions, by means of sequences of the HIV2 virus obtained from lambda-ROD4, lambda-ROD35 and E2 clones (Clavel et al. (1986-Nature, 324, p. 691.) and nick-translated.

The hybridization was performed in 5 × SSC at 50°C and the washes in 2 × SSC at 50°C. Only one clone containing all the viral sequences was obtained. This clone is designated by lambda-SIV-1. The insert of the lambda-SIV-1 phage measures 16.5 kb in total and comprises an integrated provirus from which only the first 250 bases of the left-hand LTR are missing, whereas the right-hand LTR is complete.

The integrated provirus was sequenced by the dideoxynucleotide method after subcloning of random fragments into the phage M13mp8. 300 subclones were analysed.

cDNA fragments obtained from the Lambda SIV-1 clone inserted into plasmids pSIV-1.1 and pSIV-1.2 were deposited at CNCM on 15 April 1987, under the numbers I-658 (pSIV-1.1) and I-659 (pSIV-1.2).

The results have been presented in the figures described below.

Figure 1B represents the nucleotide sequence of the SIV viral genome and the sequences which are deduced therefrom for the viral proteins corresponding to the products of the gag, pol, env, Q, X, R, tat, art, F genes.

Figures 3 to 11 and Figure 1C represent comparisons of the theoretical products of the viral genes and the LTRs between HIV2 and SIVmac (λSIV-1).

The cDNA fragments deduced from the cDNA derived from the whole SIV-1 genome which contain one or more sequences derived from the complete sequence of cDNA and which encode valuable peptides of the invention are also described in the present application. These sequences are indicated in Figure 1B, and in Figure 1C in the case of the LTR sequence of the virus.

The nucleic sequences of the SIV cDNA were aligned with the nucleic sequences of the HIV-2 ROD virus in the case of the LTR sequence (Figure 1C). This presentation, which occurs for the entire genome by comparing Figure 1B with Figures 3 to 11 makes it possible to locate or deduce the nucleic acids having essential structural elements common to the two viruses.

The present application also describes the use of the cDNAs derived from SIV or fragments thereof (or

recombinants containing them) as probes for diagnosis of the presence or not of HIV-2 virus in samples of sera or other biological fluids or tissues obtained from patients suspected of being carriers of the HIV-2 virus. These probes are preferably also labelled (radioactive, enzymatic or fluorescent markers and the like). Probes particularly valuable for implementing the process for the diagnosis of the HIV-2 virus or of a variant of HIV-2 may be characterized in that they comprise all or a fraction of the cDNA complementary to the SIV virus genome or alternatively especially the recombinant fragments contained in various clones.

The probes which may be used in this process for the diagnosis of the HIV-2 virus and in diagnostic kits are not in any way limited to the probes described above. They comprise, on the contrary, all the nucleotide sequences derived from the genome of the SIV virus, of a variant of SIV or of a virus related by its structure, provided that they permit the detection, in biological fluids from persons capable of developing AIDS, of antibodies directed against an HIV-2 or of a virus which is related to it.

The detection may be carried out in any manner known per se. It may comprise the placing of these probes in contact either with the nucleic acids obtained from the cells contained in these sera or other biological media, for example spinal fluids, salivas and the like. It may also comprise a placing of these probes into contact with these media themselves provided that their nucleic acids have been rendered accessible to hybridization with these probes and this under conditions which permit hybridization between these probes and these nucleic acids. The final step of the <u>in vitro</u> diagnosis then comprises the detection of the hybridization which

may be produced. The abovementioned diagnosis using hybridization reactions can also be performed by means of mixtures of probes originating from an HIV-2 and from an SIV-1 or from an HIV-1, from an HIV-2 and from an SIV, respectively, provided that it is not necessary to differentiate between the type of virus desired.

Generally, the process for the diagnosis of the presence or otherwise of the HIV-2 virus or of a variant in samples of sera or other fluids or tissues obtained from patients suspected of being carriers of the HIV-2 virus comprises the following steps:

1/ at least one hybridization step performed under stringent conditions by placing the DNA of cells from the sample from the suspected patient into contact with one of the abovementioned labelled probes on an appropriate membrane,

2/ washing the said membrane with a solution which ensures the preservation of these stringent conditions for the hybridization,

3/ detection of the presence or not of the HIV-2 virus by an immunodetection method.

Alternatively, the abovementioned hybridization is performed under non-stringent conditions and the washing of the membrane is carried out under conditions adapted to those for the hybridization.

The application also describes the nucleic acids corresponding to sequences placed in analogous regions of variants of SIV as well as all nucleic acids whose modifications might result from the exploitation of the degeneracy of the genetic code.

The comparative studies which have also made it possible to arrive at results relating to the core proteins, hereinafter called "gag proteins" and to the envelope proteins, hereinafter called "env proteins" have

also been reported in European Patent Application No. 87/400.151.4, which has already been mentioned. These results show that the core proteins (gag proteins) in HIV-2 have less pronounced differences, relative to those of the HIV-1 viruses, than the envelope proteins (env proteins). Overall, the env proteins in HIV-2 have proved to have extremely weak, if not non-existent, immunological relationships with the corresponding env proteins of HIV-1 viruses.

On the other hand, comparative studies carried out between the structures of the cDNA sequences of the HIV-2 and SIV viruses make it possible to reveal certain common characteristics which appear at the level of the proteins.

Overall, the proteins of HIV-2 and SIV-1 show strong immunological relationships.

The major envelope glycoprotein of HIV-2 proved to be more immunologically related to the major envelope glycoprotein of SIV than to the major envelope glycoprotein of HIV-1.

These observations are valid not only with respect to the molecular weights: 130-140 kilodaltons for the major glycoproteins of HIV-2 and SIV against about 110 for the major envelope glycoprotein of HIV-1, but also with respect to the immunological properties, since sera collected from patients infected by HIV-2, and more particularly antibodies formed against gp140 of HIV-2 recognize the gp140 of SIV-1mac, whereas in similar tests the same sera and the same HIV-2 antibodies do not recognize gp110 of HIV-1. But the anti-HIV-1 sera which have never reacted with gp140 of HIV-2 precipitate a ^{35}S-cysteine-labelled 26 Kdal protein contained in extracts of HIV-2.

The major core protein of HIV-2 appears to have an average molecular weight (about 26,000) intermediate between that of p25 of HIV-1 and p27 of SIV.

These observations result from tests performed with viral extracts obtained from HIV-2 isolated from one of the abovementioned patients. Similar results were obtained with viral extracts of HIV-2 isolated from the second patient.

More detailed studies led the inventors to identify a first class of peptides having amino acid sequences which are either identical or similar to the sequences contained inside the structures of the gag and env proteins of HIV-2 or SIV or even HIV-1. These peptides are especially applicable to the diagnosis of an infection in man by the HIV-2 virus or of one of its variants.

The invention relates to a peptide characterized by the following properties:

- it is recognized by antibodies present in the serum of a patient infected with a human retrovirus HIV-2, the said antibodies recognizing the major envelope glycoprotein of a retrovirus HIV-2,
- it contains a number of amino acid residues not exceeding 40.

The invention also relates to a peptide characterized by the following properties:

- it is recognized by antibodies present in the serum of a patient infected with a human retrovirus HIV-2, the said antibodies recognizing the major envelope glycoprotein of a retrovirus HIV-2,
- it is not recognized by antibodies present in the serum of a patient infected with a human retrovirus

HIV-1, the said antibodies recognizing the major envelope glycoprotein of a retrovirus HIV-1,

- it contains a number of amino acid residues not exceeding 40.

In this regard, the present invention also relates to diagnostic processes and compositions for the in vitro detection of antibodies directed against an HIV-2 virus or of its variants, more particularly in biological samples, especially sera of patients having been subjected to an infection by the HIV-2 virus, some of these peptides permitting a particularly high discrimination between infections due to HIV-2 viruses and HIV-1 viruses.

These detailed studies have also led to the possibility of synthesizing immunogenic peptides or peptides capable of being rendered immunogenic, which have structural characteristics making it possible to induce in vivo the production of antibodies capable of recognizing env proteins both in HIV-1 and in HIV-2 and, at least for some of these peptides, of binding to both HIV-1 viruses and HIV-2 viruses, more particularly for the purpose of neutralizing them. The use of these latter types of peptides is therefore particularly recommended for the production of active ingredients of vaccines against the HIV viruses, therefore against AIDS.

In order to designate below the amino acid residues entering into the constitution of the peptides according to the invention, there will be used, for those of the amino acids having a univocal meaning, the international nomenclature designating each naturally occurring amino acid by a single letter (capital letter) according to the table of correspondences below:

M Methionine

L	Leucine
I	Isoleucine
V	Valine
F	Phenylalanine
S	Serine
P	Proline
T	Threonine
A	Alanine
Y	Tyrosine
H	Histidine
Q	Glutamine
N	Asparagine
K	Lysine
D	Aspartic acid
E	Glutamic acid
C	Cysteine
W	Tryptophan
R	Arginine
G	Glycine

When it is possible for an amino acid, because of its position inside the amino acid chain characteristic of a determined peptide, to take several meanings, it can either be designated by a "-", if it can have any meaning, or by a small letter when this amino acid can have a limited number of preferred meanings, this number being, however, always greater than 1. In this latter case, the possible meanings of this small letter will be always specified in relation to the peptide to which it belongs.

In order to facilitate reading, peptides will be designated by an abbreviation <u>env</u> or <u>gag</u> followed by a numerical index, by reference to amino acid sequences contained, depending on the case, either in the <u>env</u> proteins or in the <u>gag</u> proteins of some HIV-1, HIV-2 or

SIV viruses. Reference will again be made thereto in what follows.

Finally, in the following definitions

- the groups X represent either a free or amidated NH_2 group, especially by one or two alkyl groups comprising 1 to 5 carbon atoms, or a peptide group comprising 1 to 5 amino acids, of which the N-terminal amino acid itself has a free or amidated NH_2 group as indicated above, and
- the groups Z represent either a free -OH or alkoxyl group and containing, in this case, an alkyl group comprising 1 to 5 carbon atoms, or a peptide group comprising 1 to 5 amino acids, of which the C-terminal amino acid itself has a free -OH or alkoxyl group, as indicated above, the groups of 1 to 5 amino acids, where appropriate contained in X or Z or in both at the same time, being such that their presence is not incompatible with the preservation, for the most part, of the immunological, where appropriate immunogenic, properties of the peptides which are devoid thereof.

The peptides according to the invention, which have immunological properties in common with antigens of HIV-2 and, for some of them, also with antigens of HIV-1 or of its variants, are characterized in that they also have a peptide structure in common with the antigens of SIV. Advantageously, these peptides normally comprise at most 40 amino acid residues.

Preferred peptides are the following:

<u>env1</u>

XRV-AIEKYL-DQA-LN-WGCAFRQVCZ

<u>env2</u>

X-LE-AQI-QQEKNMYELQKLNZ

env3
XELGDYKLVEITPIG-APT--KR-----Z
env4
X----VTV-YGVP-WK-AT--LFCA-Z
env5
X---QE--L-NVTE-F--W-NZ
env6
XL---S-KPCVKLTPLCV--Z
env7
X---N-S-IT--C-K----Z
env8
X-I---YC-P-G-A-L-C-N-TZ
env9
X------A-C------W--Z
env10
X-G-DPE------NC-GEF-YCN-----NZ
env11
X-----C-IKQ-I------G---YZ

More particularly, the invention relates to the following peptides:

env1
XRV-AIEKYL-DQA-LN-WGCAFRQVCZ
env2
X-LE-AQIQQEKNMYELQKLNZ
env3
XELGDYKLVEITPIG-APT--KR-----Z
env4
X----VTV-YGVP-W--AT--LFCA-Z
env5
X----E--L-NVTE-F--W-NZ
env6
XL---S-KPCVKL-PLC---Z
env7
X---N-S-I---C-K----Z
env8
X-I---YC-P-G-A-L-C-N-TZ
env9
X------A-C------W--Z

env10

X-G-DPE------NC-GEF-YC------NZ

env11

X-----C-I-Q-I------G---YZ

Advantageous peptides corresponding to the preceding ones, represent the following formulae:

env1

XRVTAIEKYLQDQARLNSWGCAFRQVCZ, or

XRVTAIEKYLKDQAQLNAWGCAFRQVCZ

env2

XSLEQAQIQQEKNMYELQKLNSWZ, or

XLLEEAQIQQEKNMYELQKLNSWZ

env3

XELGDYKLVEITPIGFAPTKEKRYSSAHZ, or

XELGDYKLVEITPIGLAPTNVKRYTTG-Z

(It will be noticed that the peptides env1, env2, env3 show the very strong relationship between HIV-2 and SIV-1. Indeed, the first peptide is included in the HIV-2 genome and the second, in that of SIV-1).

env4

XabcdVTVeYGVPfWogAThiLFCAjZ

in which the letters from a to j can have the following meanings:

a is C, E or D

b is T, K, D, N or I

c is Q or L

d is Y or W

e is F or Y

f is T, V or A

g is N or E

h is I or T

i is P or T

j is T or S

o is K or R

env5

XabcoEdeLfNVTEgFhiWjNZ,

in which the letters from a to j can have the following meanings:

a is D or P

b is D or N

c is Y or P

d is I, V, I or L

e is T, V, E or A

f is V, G or E or -

g is A, N, G or S

h is D or N

i is A or M

j is N, K or E

o is Q or S

env6

XLabcSdKPCVKLoPLCuefKZ,

in which the letters from a to f can have the following meanings:

a is F or W

b is E or D

c is T or Q

d is I or L

e is A, S or T

f is M or L

o is T or S

u is V or I

env7

XabCNxSyIocdCeKfghiZ,

in which the letters from a to i and x and y can have the following meanings:

a is N or T or I

b is H or S or N

c is E or Q

d is S, A or C

e is D or P

f is H, V or D

g is Y or S

h is W or F

i is D or E

x is T or R

Y is V or A

o is T or Q

env8

XaIbcdYCxPeGfAgLhCiNjTZ,

in which the letters from a to k and x can have the following meanings:

a is A or P

b is R or P

c is F, I or C

d is R or H

e is P or A

f is Y or F

g is L or I

h is R or K

i is - or N

j is D or K

x is A or T

env9

XwabcxyAdCefghizWjkZ,

in which the letters from a to k and x to z can have the following meanings:

a is K or - or E
b is R or -
c is P or M or I
d is W or H or Y
e is W or N or T or R
f is F or I
g is K or S or N or G
h is G or R or E
i is - or A or T
j is K or N or D or S
k is D or A or N or K or E
w is N, D or I
x is R or G or K
y is Q or K or R
z is K or E or Q or N

env10

XaGbDPEcdefghNCiGEFjYCokxlmnNz,

in which the letters from a to n and x can have the following meanings:

a is K or - or G
b is S or G or -
c is V or I
d is A or V or T
e is Y or T or M or F
f is M or H
g is W or S
h is T or F
i is R or G
j is L or F
o is N or K
k is M or S
l is W or Q or K or G
m is F or L
n is L or F

x is T or S or N

env111

XabcdnCeIoQfIxgyhizGjklYZ,

in which the letters from a to l and w to z can have the following meanings:

a is R or T or S or N

b is N or I

c is Y or T

d is A or L or V

e is H or R

f is I or F

g is T or M

h is H or Q or A

i is K or E

j is R or K

k is N or A

l is V or M

w is P or Q

x is N or K

y is W or V

z is V or T or K

o is K or R

The structure of the antigenic peptide encoded by the gag gene and designated by gag1 is also represented below

XDCKLVLKGLGaNPTLEEMLTAZ,

in which the letter a designates M or T.

It will be noticed that, generally, the amino acids having a univocal meaning (therefore represented by a capital letter corresponding to the international nomenclature) which are involved in the definitions which precede peptides according to the invention, happen to be the correspondence with identical amino acids placed in the same order in the corresponding env or gag sequences

of the env or gag protein of at least one of the HIVs or of SIV-1.

The positions of these sequences are underlined and identified inside the amino acid sequences of the env proteins of HIV-2 ROD (CNCM No. I-532) and HIV-1 BRU (CNCM No. I-232), respectively, are presented in Figure 2. Furthermore, the alignment of the amino acids of the env and gag proteins of SIV-1mac (CNCM No. I-521) and of HIV-2 ROD, respectively, are presented in Figure 3 and Figure 4.

The solid lines which appear in certain locations of these sequences are intended to underline that some amino acids contained in these sequences have been deliberately deleted at the level of the presentation so as to allow the alignment of amino acids respectively identical (marked with an asterisk in this case) or of two vertical points on the same vertical line in the corresponding protein sequences of HIV-1 and HIV-2 on the one hand, of SIV and HIV-2 on the other hand.

In addition to the abovementioned peptides, the invention also relates to the peptides modified by insertion and/or deletion and/or substitution of one or more amino acids, provided that the antigenic or immunogenic properties of the said peptides are not modified, or that the properties of recognizing the antigen or the antibody with the said peptides are not substantially modified.

In a particularly preferred embodiment, the invention relates to peptides having immunological properties in common with the peptide skeleton of the envelope glycoprotein of viruses of the HIV-2 class, these peptides containing a number of amino acid residues not exceeding 40.

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